

AMENDMENT

In the Claims:

Please amend claims 30, 33, 38, and 39, as shown below.

1-18. (Cancelled)

19. **(Withdrawn)** A polypeptide, characterized by

- (a) derived from HCV polymerase NS5B having an HCV polymerase activity;
- (b) consisting of an amino acid sequence X-Y;

wherein X comprises a consecutive amino acid sequence which is a portion of the NS5B, an N-terminal amino acid of X is the amino acid residue 1 (Ser) of the NS5B, and a C-terminal amino acid of X is an amino acid residue selected from the group consisting of amino acid residues 531 (Lys) to 570 (Arg) of the NS5B;

wherein one or more amino acids in the amino acid sequence of X may be modified, and methionine residues in the amino acid sequence of X may be replaced by selenomethionine residues;

wherein Y comprises a carboxyl group or an amino acid sequence which is not derived from NS5B.

20. **(Withdrawn)** The polypeptide of claim 19, wherein the C-terminal amino acid residue of X is an amino acid residue selected from the group consisting of 536 (Leu) to 552 (Val) of the NS5B.

21. (Withdrawn) The polypeptide of claim 20, wherein the C-terminal amino acid residue of X is an amino acid residue selected from the group consisting of 536 (Leu) to 544 (Gln) of the NS5B.

22. (Withdrawn) The polypeptide of claim 20, wherein the C-terminal amino acid residue of X is an amino acid residue selected from the group consisting of 531 (Lys) to 544 (Gln) of the NS5B.

23. (Withdrawn) The polypeptide of claim 19, wherein methionine residues in the amino acid sequence of X are replaced by selenomethionine residues.

24. (Withdrawn) The polypeptide of claim 19, wherein Y is an amino acid sequence not derived from NS5B, and said amino acid sequence is suitable for column purification.

25. (Withdrawn) The polypeptide of claim 19, wherein the NS5B comprises an amino acid sequence of SEQ ID NO: 1.

26. (Withdrawn) The polypeptide of claim 19, wherein said polypeptide is identified by three-dimensional structural coordinates shown in a table selected from the group consisting of Table 2 and Table 3.

27. (Withdrawn) A crystal comprising the polypeptide of claim 19.

28. (Withdrawn) A DNA encoding the polypeptide of claim 19.

29. (Withdrawn) A method for determining three-dimensional structural

coordinates of a variant of HCV polymerase NS5B by the molecular replacement method using a three-dimensional structure coordinate of said NS5B.

30. **(Currently amended)** A method for identifying a HCV polymerase inhibitor, said method comprising:

determining the complementarity of a test compound with an active site and/or RNA binding cleft of a polypeptide using a three-dimensional structural coordinate of said polypeptide or its part and a three-dimensional structural coordinate of said test compound,

wherein said polypeptide is derived from an NS5B HCV polymerase, has an NS5B HCV polymerase activity, and consists of an amino acid sequence X-Y, wherein X is a consecutive amino acid sequence which is a portion of NS5B, the N-terminal amino acid of X is a serine residue corresponding to amino acid residue 1 of NS5B, and the C-terminal amino acid residue of X is ~~any one of~~ selected from amino acid residues 531 (~~Lys~~) to, 536, 544, and 570 (~~Arg~~) of NS5B; and wherein Y is a carboxyl group or an amino acid sequence which is not derived from NS5B; ~~and wherein one or more amino acids in X may be modified~~, and wherein methionine residues in the amino acid sequence of X may be replaced by selenomethionine residues,

wherein a test compound that is complementary to said active site and/or RNA binding cleft of said polypeptide ~~is-a~~ inhibits a HCV polymerase ~~inhibitor~~ by binding to said active site and/or RNA binding cleft of said HCV polymerase.

31. **(Previously presented)** A method for identifying a HCV polymerase inhibitor, which method comprises the steps of:

- (a) performing the method of claim 30; and
- (b) determining a HCV polymerase-inhibitory activity of said HCV polymerase inhibitor.

32. **(Withdrawn)** The method of claim 29, wherein the three-dimensional structural coordinate of the polypeptide is selected from the group consisting of dimensional structural coordinates shown in a table selected from the group consisting of Table 2 and Table 3.

33. **(Currently amended)** A method for identifying a HCV polymerase inhibitor, which method comprises the steps of:

- (a) obtaining a polypeptide which is derived from an NS5B HCV polymerase, has an NS5B HCV polymerase activity, and consists of the amino acid sequence X'-Y, wherein X' is a consecutive amino acid sequence which is a portion of the NS5B, the N-terminal amino acid of X' is a serine residue corresponding to amino acid residue 1 of NS5B, and the C-terminal amino acid residue of X' is any one of selected from amino acid residues 531 (Lys) to 536, and 544 (Gln) of NS5B; and wherein Y is a carboxyl group or another amino acid sequence which is not derived from NS5B; and wherein ~~one or more amino acids in X' may be modified, and methionine residues in the amino acid sequence of X' may be replaced by selenomethionine residues;~~

(b) determining the HCV polymerase activity of said polypeptide by reacting said polypeptide obtained in step (a) with a template RNA and substrates in the presence of a test compound;

(c) determining the HCV polymerase activity of said polypeptide by reacting polypeptide obtained in step (a) with a template RNA and substrates in the absence of said test compound; and,

(d) comparing the HCV polymerase activity determined in step (b) with the HCV polymerase activity determined in step (c).

34. **(Withdrawn)** An HCV polymerase inhibitor, identified by the method of claim 30.

35. **(Withdrawn)** An HCV polymerase inhibitor that inhibits the HCV polymerase activity of HCV polymerase NS5B by acting on a boundary between Thumb and Palm domains of NS5B.

36. **(Withdrawn)** The HCV polymerase inhibitor of claim 35, wherein said inhibitor is a compound represented by the formula, Z-Asp-Leu-Ser-Gly-Trp-Phe-Z', wherein Z is Leu or a hydrophilic group, and Z' is Val or a hydrophilic group.

37. **(Canceled)**

38. (Currently Amended) The method according to claim 31, wherein the C-terminal amino acid residue of X is selected from the group consisting of amino acid residues 531, 536, 544 and 570 of NS5B.

39. (Currently Amended) The method according to claim 33, wherein the C-terminal amino acid residue of X' is selected from the group consisting of amino acid residues 531, 536, 536 and 544 of NS5B.